Remarks

With this response, Claims 35, 51, 79, and 87 have been amended, claims 67-72 and 101-104 have been cancelled, and new claims 105-112 have been added. No new matter enters by way of the present amendments. As such, Claims 35-66, 73-100, and 105-112 are currently pending and under consideration. The claims are presented as renumbered by the Examiner in the Office Action mailed November 4, 2003 (Paper No. 41).

More specifically, Claims 35 and 73 have been amended to recite "a subject desirous or in need of reducing food intake." Claims 51 and 87 have been amended to recite "a subject desirous or in need of reducing appetite." New claims 105-112 recite "a subject desirous or in need of reducing body weight." Support for these recitations may be found, e.g., at page 13 lines 12-19, page 37 lines 17-19, and page 38 lines 9-10 of the specification. As such, no new matter enters by way of the amendments.

I. Examiner Interview

Applicants thank Examiners Low and Mohamed for their courtesy in allowing Applicants to conduct an Examiner Interview (the "Interview") on February 6, 2004. Applicants further thank the Examiners for their suggestions and insights. In attendance at the Interview (in person and via telephone) were Examiners Low and Mohamed, and Applicants' representatives, David Marsh, Milan Vinnola, Molly Holman, and Dr. Andrew Young..

During the Interview, Applicants explained, and the Examiners agreed that Navarro et al. ("Navarro") did not disclose or suggest the use of exendin-3 and that Navarro did not disclose or suggest the combined use of GLP-1 (7-36) amide and exendin-4. Further, it was agreed that Navarro did not disclose or suggest the peripheral administration of an exendin, and that "the prior art of record either singularly or in combination does not teach the claimed invention." See Interview Summary, Paper No. 16. Applicants also agreed to provide an explanation of the term "peripheral" and to file a terminal disclaimer upon an indication of allowable subject matter.

II. Rejection under 35 U.S.C. § 103(a)

Claims 35-66 and 73-100 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Navarro taken with Eng (US Patent No. 5,424,286) and WO 96/40196. This

rejection is respectfully traversed, and to the extent that it applies to the new claims, reconsideration is requested for at least the reasons that follow.

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. The teaching or suggestion to make the claimed combination must be found in the prior art, and not be based on applicant's disclosure. *See* M.P.E.P. §§ 2143.01 and 2143.03.

The present invention is drawn to methods for reducing food intake and methods for reducing the appetite of a subject. The methods of the present invention generally comprise peripherally administering to a subject an effective amount of an exendin. In contrast, Navarro discusses the intracerebroventricular (I.C.V.) administration of exendin (9-39), a GLP-1 antagonist, prior to the I.C.V. administration of GLP-1 (7-36) amide or the I.C.V. administration of exendin-4 for the experimental purpose of attempting to antagonize the effect of GLP-1 or exendin-4 with exendin (9-39).

As discussed during the Interview, and acknowledged by the Examiners, based only on a showing of physiological effect by a molecule, such as exendin, following administration to the central nervous system, a person skilled in the art would not be able to predict whether the molecule exerts the same physiological effect when peripherally administered, or vice versa. Nowhere in the cited art is there teaching, disclosure, or suggestion that a molecule such as exendin has the same physiological effect when administered to the central nervous system (e.g., I.C.V.) vis-à-vis administered peripherally.

Moreover, as discussed and acknowledged during the interview, just because a particular peptide, such as exendin-4 or GLP-1, has a particular effect upon I.C.V. administration does not teach that a similar effect will occur upon peripheral administration. Indeed, Navarro itself shows such unpredictability with regard to GLP-1 (7-36) amide. Navarro teaches that subchronic intraperitoneal (i.e., a type of peripheral) administration of GLP-1 (7-36) amide did not modify food and water intake, although a dose-dependent loss of body weight gain was observed 24 hours after acute administration of the higher dose of the peptide (i.e., 1,000 ng peptide /100 g of body weight). By contrast, the I.C.V. administration of GLP-1 (7-36) amide

produced a biphasic effect on food intake characterized by an increase in the amount of food intake after acute I.C.V. delivery of 100 ng of the peptide versus a marked reduction in food ingestion and water intake with the 1,000 and 2,000 ng doses of the peptide. Navarro at Abstract and FIGS. 2 and 3.

As agreed to during the Interview, Navarro does not disclose or suggest the peripheral administration of an exendin, much less the ability of exendins to reduce the food intake or appetite of a subject following peripheral administration. Eng and WO 96/40196 do nothing to remedy the deficiencies of Navarro in this respect. Neither secondary reference teaches, discloses, or suggests the use or ability of exendins to reduce the food intake or appetite of a subject following peripheral administration. As such, Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness, as required by 35 U.S.C. § 103. Even assuming, *arguendo*, that a *prima facie* case of obviousness has been established, Navarro in fact teaches away from the present invention based on the finding that peripheral administration of GLP-1 (7-36) amide does not "modify food and water intake."

For at least the foregoing reasons, it is respectfully submitted that all of the pending claims are non-obvious over the prior art of record. As such, withdrawal of this rejection is respectfully requested.

III. Rejection under 35 U.S.C. § 112, First Paragraph

Claims 35-66 and 73-100 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly disclosing subject matter not described in the specification. Specifically, the Office alleges that the original specification does not appear to support peripherally administering or peripheral administration. Paper No. 41 at page 11. Applicants respectfully disagree.

"Peripheral" administration is well known to be the opposite of direct (or outside of) "central" administration to the central nervous system ("CNS," e.g., I.C.V.), as discussed by Dr. Young during the Interview. In fact, the present specification discusses "peripheral" administration as opposed to "central" (e.g., I.C.V.) administration, for example, at page 5 line 21 to page 6 line 4 of the specification:

> GLP-1 administered by intracerebroventricular injection inhibits food intake in rats. . . .
> GLP-1 does not inhibit food intake in mice when administered by peripheral injection.
> (Citations omitted)

"Peripheral" administration is further supported in the specification. See, for example, specific reference to "peripheral injection" in original claim 4, and discussion of the predominate forms of peripheral administration throughout the specification, e.g., "Compositions useful in the invention may conveniently be provided in the form of formulations suitable for parenteral (including intravenous, intramuscular and subcutaneous) or nasal or oral administration" (page 33 lines 9-12 of the specification); "Compounds useful in the invention can be provided as parenteral compositions for injection or infusion" (page 34 lines 4-5); "Administration may be by injection, preferably subcutaneous or intramuscular" (page 38 lines 13-14); "Orally active compounds may be taken orally" (page 38 lines 14-15). Additionally, specific examples of peripheral administration—intraperitoneal injection—are disclosed in Examples 1 to 4 at pages 39-44 of the specification.

Applicants submit that "peripherally administering" and "peripheral administration" are both disclosed to one of ordinary skill in the art and respectfully request the withdrawal of this rejection.

Conclusion

In view of the above, each of the presently pending claims is believed to be in immediate condition for allowance. Accordingly, the Office is respectfully requested to withdraw the outstanding objection and rejection of the claims, and to pass this application to issue. The Office is encouraged to contact the undersigned at (202) 942-6111 should any additional information be necessary for allowance.

Respectfully submitted,

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